23. (Amended) The yeast cell of claim 22 wherein the DNA binding protein is selected from the group consisting of a mammalian steroid receptor and bacterial LexA protein.

29. (Amended) A method of detecting the interaction of a first peptide and a second peptide of a peptide binding pair in the presence of a test sample, comprising:

(i) culturing at least one yeast cell, wherein the yeast cell comprises;

a) a nucleotide sequence encoding a first heterologous fusion protein comprising the first peptide or a segment thereof joined to a transcriptional activation protein DNA binding domain;

b) a nucleotide sequence encoding a second heterologous fusion protein comprising the second peptide or a segment thereof joined to a transcriptional activation protein transcriptional activation domain;

wherein binding of the first peptide or segment thereof and the second peptide or segment thereof reconstitutes a transcriptional activation protein; and

c) a luciferase gene activated under positive transcriptional control of the reconstituted transcriptional activation protein;

(ii) incubating the test sample with the yeast cell under conditions suitable to detect the selected phenotype; and

(iii) detecting the interaction of the first peptide and the second peptide by determining the level of expression of the luciferase gene.

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39. (Amended) The method of claim 38, wherein the yeast cell is *Saccharomyces cerevisiae*.

43. (Amended) A method for determining whether a test sample interacts with a first or second peptide of a peptide binding pair, comprising:

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(i) culturing at least one first yeast cell, wherein the first yeast cell comprises;

a) a nucleotide sequence encoding a first heterologous fusion protein comprising the first peptide or a segment thereof joined to a transcriptional activation protein DNA binding domain;

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b) a nucleotide sequence encoding a second heterologous fusion protein comprising the second peptide or a segment thereof joined to a transcriptional activation protein transcriptional activation domain;

wherein the nucleotide sequence encoding the first heterologous fusion protein is present in an effective copy number of at least 5 copies per yeast cell and the nucleotide sequence encoding the second heterologous fusion protein is present at a copy number of 1 or 2 per yeast cell;

and

wherein binding of the first peptide or segment thereof and the second peptide or segment thereof reconstitutes a transcriptional activation protein; and

c) a luciferase gene activated under positive transcriptional control of the reconstituted transcriptional activation protein;

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(ii) culturing at least one second yeast cell, wherein the second yeast cell comprises;

a) a nucleotide sequence encoding a first heterologous fusion protein comprising the first peptide or a segment thereof joined to a transcriptional activation protein DNA binding domain;

b) a nucleotide sequence encoding a second heterologous fusion protein comprising the second peptide or a segment thereof joined to a transcriptional activation protein transcriptional activation domain;

wherein the nucleotide sequence encoding the second heterologous fusion protein is present in an effective copy number of at least 5 copies per yeast cell and the nucleotide sequence encoding the first heterologous fusion protein is present at a copy number of 1 or 2 per yeast cell;

and

wherein binding of the first peptide or segment thereof and the second peptide or segment thereof reconstitutes a transcriptional activation protein; and

c) a luciferase gene activated under positive transcriptional control of the reconstituted transcriptional activation protein;

(iii) incubating a test sample with the first and second yeast cells under conditions suitable to detect luciferase activity;

(iv) detecting the luciferase activity produced by the first and second yeast cells; and

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(v) comparing the detected luciferase activity of the first and second yeast cells, wherein lower luciferase activity in one of the yeast cells compared to the other yeast cell indicates that the test sample binds to the heterogeneous fusion protein encoded by the nucleotide sequence present at a copy number of 1 or 2 in that yeast cell exhibiting lower luciferase activity, thereby affecting the binding interaction of the peptide binding pair.

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44. (Amended) The method of claim 43 wherein either or both of the first and second yeast cells further comprises at least one endogenous nucleotide sequence selected from the group consisting of a nucleotide sequence encoding the transcriptional activation protein DNA binding domain, and a nucleotide sequence encoding the transcriptional activation protein transcriptional activation domain wherein at least one of the endogenous nucleotide sequences is inactivated by reconstitution or deletion.

52. (Amended) The method of claim 43 wherein either or both of the first and second yeast cells comprises:

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a) a nucleotide sequence encoding a first heterologous fusion protein comprising a first peptide of a peptide binding pair that bind through extracellular interaction in their natural environment, or a segment thereof, joined to a transcriptional activation protein DNA binding domain;

b) a nucleotide sequence encoding a second heterologous fusion protein comprising a second peptide of the binding pair, or a segment thereof, joined to a transcriptional activation protein transcriptional activation

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domain;

wherein binding of the first peptide or segment thereof and the second peptide or segment thereof reconstitutes a transcriptional activation protein; and

c) a luciferase gene activated under positive transcriptional control of the reconstituted transcriptional activation protein.

58. (Amended) A method of simultaneously detecting the interaction of two different peptide binding pairs in the presence of at least one test sample, wherein the first peptide binding pair comprises a first peptide and a second peptide, and wherein the second peptide binding pair comprises a third peptide and a fourth peptide, comprising:

(i) culturing at least one yeast cell, wherein the yeast cell comprises;

a) a nucleotide sequence encoding a first heterologous fusion protein comprising the first peptide or a segment thereof joined to a DNA binding domain of a first transcriptional activation protein;

b) a nucleotide sequence encoding a second heterologous fusion protein comprising the second peptide or segment thereof joined to a transcriptional activation domain of the first transcriptional activation protein;

c) a nucleotide sequence encoding a third heterologous fusion protein comprising the third peptide or segment thereof joined to a DNA binding domain of a second transcriptional activation protein;

d) a nucleotide sequence encoding a fourth heterologous fusion protein comprising the fourth peptide or a segment thereof joined to

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a transcriptional activation domain of the second transcriptional activation protein;

wherein binding of the first peptide or segment thereof and the second peptide or segment thereof reconstitutes the first transcriptional activation protein, and binding of the third peptide or segment thereof and the fourth peptide or segment thereof reconstitutes the second transcriptional activation protein;

e) a first luciferase gene activated under positive transcriptional control of the first reconstituted transcriptional activation protein;

f) a second luciferase gene activated under positive transcriptional control of the second reconstituted transcriptional activation protein; and

(ii) incubating the at least one test sample with the yeast cell under conditions suitable to detect luciferase activity; and

(iii) detecting the interaction of the first peptide and the second peptide by determining the level of expression of the first luciferase gene and detecting the interaction of the third peptide and the fourth peptide by determining the level of expression of the second luciferase gene.

64. (Amended) The method of claim 63 wherein the peptide is a growth factor selected from the group consisting of epidermal growth factor, nerve growth factor, leukemia inhibitory factor, fibroblast growth factor, platelet-derived growth factor, vascular endothelial growth factor, tumor necrosis factor, oncostatin M, ciliary neurotrophic factor, erythropoietin, steel factor, placental lactogen, and TGF.

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